Claims

1. Use of at least one oligonucleotide or its active derivative for the preparation of a pharmaceutical composition for inhibiting the formation of metastases in cancer treatment.

2. Use according to claim 1 wherein the oligonucleotide is an antisense oligonucleotide inhibiting the synthesis of proteins involved in the formation of metastases.

3. Use according to claim 1 or 2 wherein the oligonucleotide is an antisense oligonucleotide inhibiting the production of TGF-beta1, TGF-beta2, TGF-beta3, cell-cell adhesion molecules (CAMs), integrins, selectines, metalloproteases (MMPs), their tissue inhibitors (TIMPs) and/or interleukin 10.

4. Use according to any of claims 1 to 3 wherein the oligonucleotide is identified in the sequence listing under SEQ ID NO.1 to 68, 69 to 107 or is identified in the examples 19 to 24.

5. Use of oligonucleotides according to any of claims 1 to 4 wherein the oligonucleotide is identified in the sequence listing under SEQ ID NO. 1, 5, 6, 8, 9, 14, 15, 16, 28, 29 30, 34, 35, 36, 40, 42.

6. Use according to any of claim 1 to 5 wherein the cancer is selected from the group of bile duct carcinoma, bladder carcinoma, brain tumor, breast cancer, bronchogenic carcinoma, carcinoma of the kidney, cervical cancer, choriocarcinoma, cystadenocarcinoma, cervical carcinoma, colon carcinoma, colorectal carcinoma, embrional carcinoma, endometrial cancer, epithelial carcinoma, esophageal cancer, gallbladder cancer, gastric cancer, head and neck cancer, hepatocellular cancer, liver carcinoma, lung carcinoma, medullary carcinoma, non-small-cell bronchogenic/lung carcinoma, ovarian cancer, pancreas carcinoma, papillary carcinoma, papillary adenocarcinoma, prostate cancer, small intestine carcinoma, rectal cancer, renal cell carcinoma, sebaceous gland carcinoma, skin cancer, small-cell bronchogenic/lung carcinoma, soft tissue cancer, squamous cell carcinoma, testicular carcinoma, uterine cancer, acoustic neuromas, neurofibromas, trachomas, and pyogenic granulomas; pre-malignant tumors, blastoma,

Ewing´s tumor, craniopharyngioma, ependymoma, medulloblastoma, hemangioblastoma, medullablastoma, melanoma, mesothelioma, neuroblastoma, neurofibroma, pinealoma, retinoblastoma, retinoblastoma, sarcoma (including angiosarcoma, chondrosarcoma, endothelialsarcoma, fibrosarcoma, gliosarcoma, leiomyosarcoma, liposarcoma, lymphangioandotheliosarcoma, lyphangiosarcoma, melanoma, meningioma, myosarcoma, osteogenic sarcoma, osteosarcoma), seminoma, trachomas, Wilm´s tumor and/or myeloma, multiple.

7. Use according to any of claim 1 to 5 wherein the cancer is selected from the group of prostata cancer, colon carcinoma, endometrial cancer, esophageal cancer, hepatocellular cancer, non-small-cell lung carcinoma, ovarian cancer, pancreas carcinoma and soft tissue cancer or is selected from the group of melanoma, renal cancer, leukaemia, lymphoma, osteosarcoma, mesothelioma, myeloma multiple and or bladder cancer.

8. Use of oligonucleotides or their active derivatives for the preparation of a pharmaceutical composition for the treatment of prostate cancer, bladder carcinoma, colon cancer, endometrial cancer, hepatocellular carcinoma, leukemia, lymphoma, melanoma, non-small cell lung cancer (NSCLC), ovarian cancer, pancreatic cancer or is selected from the group of melanoma, renal cancer, leukaemia, lymphoma, osteosarcoma, mesothelioma, myeloma multiple and or bladder cancer.

9. Use according to claim 8 wherein the oligonucleotide is an antisense oligonucleotide inhibiting the production of transforming growth factor beta 1 (TGF-beta 1), TGF-beta 3 and/or interleukin 10 or is inhibiting the production of transforming growth factor TGF-beta2

10. Use according to claim 9 wherein the oligonucleotide is identified in the sequence listing under SEQ ID NO. 1 to 21 or 49 to 68, 22 to 48 or 69 to 107 or is identified in examples 19 to 24.

11. Antisense-oligonucleotide or its active derivative, selected from the group of IL-10 antisense oligonucleotides identified in the sequence listing under Seq. ID. NO 49 to 68 or is identified in example 22.

12. Process of manufacturing the antisense oligonucleotide or its active derivative according to claim 11 by adding consecutive nucleosides and linker stepwise or by cutting the oligonucleotide out of longer oligonucleotide chain.

13. Process according to claim 12 by using phosphite triester chemistry growing the nucleotide chain in 3´-5´direction wherein the respective nucleotide is coupled to the first nucleotide that is covalently attached to the solid phase comprising the steps of

- cleaving 5´DMT protecting group of the previous nucleotide
- adding the respective nucleotide for chain prolongation
- modifying phosphite groups subsequently cap unreacted 5´-hydroxyl groups and cleaving the oligonucleotides from the solid support
- followed by working up the synthesis product

14. Pharmaceutical composition comprising an antisense oligonucleotide identified in the sequence listing under Seq. ID. NO 49 to 68 or is identified in example 22.

15. Use of the antisense oligonucleotide according to claim 10 for the preparation of a pharmaceutical composition for the treatment of cancer and/or metastases.

16. Use of a TGF-beta 2 antagonist for the preparation of a pharmaceutical composition for the treatment of colon cancer, prostate cancer, melanoma, endometrial cancer, bladder cancer, ovarian cancer, pancreas cancer and/or mesothelioma

17. Use according to claim 16 wherein the antagonist is selected from the group of TGF-beta2 binding proteins, TGF-beta receptor related inhibitors, Smad inhibitors TGF-beta2 binding peptides, TGF-beta antibodies, regulators of TGF-beta2 expression, TGF-beta2 antisense oligonucleotides or its active derivatives.

18. Use according to claim 17 wherein the oligonucleotide is identified in the sequence listing under SEQ ID NO 22 to 48 or is identified in example 20, example 23 or example 24.

19. Use of a TGF-beta 2 antagonist for the treatment of colon cancer, prostate cancer, melanoma, endometrial cancer, bladder cancer, ovarian cancer, pancreas cancer and/or mesothelioma.

20. Use of at least one oligonucleotide or its active derivative for the treatment of metastases.

21. Use of at least one oligonucleotide or its active derivatives for the treatment of colon cancer, prostate cancer, melanoma, bladder cancer, endometrial cancer, esophageal cancer, hepatocellular cancer, non –small-cell lung cancer, ovarian cancer, osteosarcoma, mesothelioma, renal cancer, myeloma multiple, pancreas carcinoma, leukaemia, lymphoma and/or soft tissue cancer.

22. Use of at least one antisense oligonucleotide identified in the sequence listing under SEQ ID NO 49 to 69 or identified in example 22 for the treatment of cancer and/ metastases.